CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
ORTHO-BENZYL-PARA-CHLOROPHENOL
Chemical Code # 000522, Tolerance # 50306
SB 950 # 348

December 2, 1987
Revised: 8/14/91, 12/19/91, 11/29/95, 4/25/97, 2/11/00

I. DATA GAP STATUS

Chronic, rat:	Data gap, inadequate study, possible adverse effect indicated.
Chronic toxicity, dog	Data gap, no study on file.
Oncogenicity, rat:	No data gap, possible adverse effect.
Oncogenicity, mouse:	Data gap, inadequate study, possible adverse effect.
Reproduction, rat:	Data gap, no study on file.
Teratology, rat:	No data gap, no adverse effect.
Teratology, rabbit:	No data gap, possible adverse effect.
Gene mutation:	No data gap, no adverse effect.
Chromosome effects:	No data gap, no adverse effect indicated.
DNA damage:	No data gap, no adverse effect.
Neurotoxicity:	Not required at this time.

Toxicology one-liners are attached.

All record numbers through 149378 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
File name: T000211
Toxicology summary revised by H. Green & M. Silva 8/14/91; Gee, 12/19/91; M. Silva, 11/29/95, 4/25/97, 2/11/00.

In accordance with the California Administrative Code Section 6198.5b, data from studies with ortho-benzyl-para-chlorophenol (SB # 348), ortho-benzyl-para-chlorophenol, potassium salt (SB # 574) and ortho-benzyl-para-chlorophenol, sodium salt (SB # 575) are grouped for review and for filling data gaps. All data are from studies using ortho-benzyl-para-chlorophenol. No data from studies using the salts are on file.

These pages contain summaries only. Individual worksheets should be reviewed as they may contain additional effects.

II. TOXICOLOGY SUMMARY

COMBINATION, RAT
(chronic/onco)

032, 045 114237, 133499 "The Chronic Gavage Study of o-Benzyl-p-Chlorophenol (CAS No. 120-32-1) in Fischer 344 Rats", (M. Hejtmancik, S.L. Grumbein, P.A. Athey, & A.C. Peters, Battelle (Columbus Division), March 1988). The test article, o-benzyl-p-chlorophenol, purity at least 95%, was administered by gavage at concentrations of 0 (corn oil), 30, 60, or 120 mg/kg and at 0 (corn oil), 60, 120, or 240 mg/kg to 80 Fischer 344 male and female rats/group, respectively. Sacrifice was scheduled at week 13, 65 and 104 for 10, 20 and 50 rats/sex/group, respectively. Systemic NOEL < 30 mg/kg (Increased urine stains in females at ≥ 60 mg/kg. Nephropathies increased in severity at ≥ 60 mg/kg. Absolute and relative kidney weights were increased in both sexes at ≥ 30 mg/kg (males) or ≥ 60 mg/kg (females). Thymus weights were decreased in males at all doses. All tested urinary enzymes were increased in males at 120 mg/kg and in females at ≥ 30 mg/kg. Urine coproporphyrin concentrations were increased and liver porphyrins were decreased at all treatment levels in both sexes of treated rats.) **Possible adverse effect.** Oncogenicity NOEL 120 mg/kg (males) and 60 mg/kg (females): There was an increase in renal tubular adenomas (high dose both sexes), carcinomas (both sexes--120 mg/kg) and transitional cell carcinomas (females) at 240 mg/kg. UNACCEPTABLE. Not upgradeable as a combined study (no ophthalmology), possibly upgradable as a oncogenicity study, upon submission of requested information (see Discussion in the report). (Kishiyama & Silva, 11/9/95)

CHRONIC, DOG

No study on file.

ONCOGENICITY, RAT

**** 032, 045, 054 114237, 133499, 149378** "The Chronic Gavage Study of o-Benzyl-p-Chlorophenol (CAS No. 120-32-1) in Fischer 344 Rats", (M. Hejtmancik, S.L. Grumbein, P.A. Athey, & A.C. Peters, Battelle (Columbus Division), March 1988). The test article, o-benzyl-p-chlorophenol, purity at least 95%, was administered by gavage at concentrations of 0 (corn oil), 30, 60, or 120 mg/kg and at 0 (corn oil), 60, 120, or 240 mg/kg to 80 Fischer 344 male and female rats/group, respectively. Sacrifice was scheduled at week 13, 65 and 104 for 10, 20 and 50 rats/sex/group, respectively. Systemic NOEL < 30 mg/kg (Increased urine stains in females at ≥ 60 mg/kg. Nephropathies increased in severity at ≥ 60 mg/kg. Absolute and relative kidney weights were increased in both sexes at ≥ 30 mg/kg (males) or ≥ 60 mg/kg (females). Thymus weights were decreased in males at all doses. All tested urinary enzymes were decreased in males at 120 mg/kg and in females at ≥ 30 mg/kg. Urine coproporphyrin concentrations were increased and liver porphyrins were decreased at all treatment levels in both sexes of treated rats.) **Possible adverse effect.** Oncogenicity NOEL 120 mg/kg (males) and 60 mg/kg (females): There was an increase in renal tubular adenomas (high dose both sexes), carcinomas (both sexes--120 mg/kg) and transitional cell carcinomas (females) at 240 mg/kg. Originally reviewed as unacceptable (Silva, 11/9/95). Upon submission of the requested oncogenicity information, the study is upgraded to acceptable as an oncogenicity study. (Kishiyama & Silva, 4/24/97)

ONCOGENICITY, MOUSE

032, 045, 053 114238, 133499, 148966 "The Chronic Gavage Study of o-Benzyl-p-Chlorophenol in B6C3F1 Mice,@ (M. Hejtmancik, M.J. Ryan, S.L. Grumbein, P.A. Athey, & A.C. Peters--Authors of original report; 3/88; Shiotsuka, R.N.--Author of supplement; 8/5/96 Battelle, Columbus, OH).

O-benzyl-p-chlorophenol (95% pure) was administered by gavage to B6C3F1 mice (70/sex/dose) at 0 (corn oil), 120, 240 or 480 mg/kg. Sacrifice was scheduled at week 13, 65 and 104 for 10, 20 and 50 mice/sex/group, respectively. Systemic NOEL < 120 mg/kg/day (Nephropathy increased at all doses in both sexes. Kidney weights in both sexes decreased at all doses in both sexes. Liver weights were increased at ≥ 240 mg/kg. Clinical signs (thin, abnormal posture, rough hair coat & hypoactivity) occurred at all doses. Body weights decreased in males (all doses) and females (≥ 240 mg/kg). Food consumption increased in both sexes at all doses.) Oncogenicity NOEL < 120 mg/kg **Possible adverse effect indicated:** There was an increase in renal adenomas and carcinomas at all doses in males (significant at ≥ 240 mg/kg. Previously reviewed as not acceptable (Silva, 11/8/95). Some of the requested data were submitted (justification for low dose, hematological data, a detailed summary of results and individual data, appendices as referenced, GLP sign-offs and an analysis of dosing solution for stability and homogeneity), however some of the tables were not readable (poor reproductions). The study remains unacceptable, but possibly upgradeable upon submission of readable copies of data tables. (Silva, 2/11/00).

REPRODUCTION, RAT

No study on file.

TERATOLOGY, RAT

** 007 027174 "Embryotoxicity (Including Teratogenicity) Study with Preventol BP Technical in the Rat." (Research and Consulting Co. Ltd., 11-27-84) Preventol BP technical (96.8% AI) in PEG at 0, 15, 75, and 375 mg/kg/day was administered by oral gavage to mated female Wistar rats (25/group) on Days 6-15 of gestation (Day 0= +sperm). Maternal effects (decreased maternal weight gain and food consumption during treatment; 3 deaths at 375 mg/kg) reported. Maternal NOEL = 75 mg/kg/day. Fetal effects (significantly reduced fetal body weight, delayed ossification) at 375 mg/kg/day. Developmental NOEL = 75 mg/kg/day. No adverse effects indicated since fetal effects were observed at the same level as maternal effects. Initially reviewed (Parker, 10-21-85) as unacceptable, upgradeable (clinical observations needed). Re-review concludes that the omission of the clinical observation data is not critical since maternal toxicity was indicated by reduced body weight gain. Change in status to ACCEPTABLE. (Parker, 11/19/87)

010 051079 "Chlorophen: Teratology Study in the Rat." (Life Science Research, Report No. 85/BTP032/054, 4-29-85) Chlorophen (97.8%) was administered by gavage to mated CD rats, 20/group, at 0 (corn oil), 100, 300, or 900 mg/kg/day on days 6 - 15 of gestation (Day 1 = +sperm). Maternal NOEL = 100 mg/kg/day (decreased body weight gain and food consumption during treatment at 300 and 900 mg/kg, increased water intake and post-dosing salivation). Developmental NOEL = ≥900 mg/kg/day, no developmental effects. UNACCEPTABLE, but upgradeable**.** No clinical observations, no necropsy observations, individual fetal data, including weights should be presented such that it is possible to associate all reported findings with individual fetuses. Shimer, 11/30/87, Becker, 12/1/87.

010 51077 Pilot study for 51079. (See 51079 worksheet for review.)

TERATOGENICITY, RABBIT

007 27173 "Segment II Teratology Study with Santophen I in Rabbits." (Bio/Dynamics Inc. 9-30-79) Santophen I (lot KK04-56, purity not stated) in 1% aqueous gum tragacanth at 0, 40, 80, and 160 mg/kg/day (all died at 300 mg/kg/day in pilot) was administered by oral gavage to mated female New

Zealand White rabbits (24/group) on Days 7-19 of gestation (Day 0= coitus observed). Maternal effects (excess deaths which may be related to dosing trauma or treatment, transient but significant decrease in body weight at 160 mg/kg) reported. Apparent Maternal NOEL= 80 mg/kg. Adverse effects in fetuses (protruding tongue but no associated skeletal defects; low frequency of various skeletal anomalies) at 40 and 80 mg/kg/day. Inadequate number of litters for evaluation at 160 mg/kg/day. Developmental NOEL not reached. UNACCEPTABLE, not upgradeable (no analysis of dosing preparation, no purity data, no clinical observation data, too few litters at high dose, unclear cause of death in high dose animals). (Aldous, 10/21/85)

007 027172 Pilot study for 27173. (See 27173 worksheet for review.)

**** 010, 034 051080, 051078 & 118537** "Chlorophen: Effects of Oral Administration Upon Pregnancy in the Rabbit," (F.W. Ross, Supplement to LSR Report #: 85/BTP033/257; LSR Ltd., Suffolk, England; 10/7/92). Chlorophen (97.9% pure) was administered by gavage to mated New Zealand White rabbits (14-21/dose) on days 6-19 of gestation at 0 (corn oil), 10, 30 or 100 mg/kg. Maternal NOEL $\geq$ 100 mg/kg (No effects were reported at any dose.) Developmental NOEL = 30 mg/kg (**Possible adverse effects:** There was an increased post-implantation loss and an increased incidence in ectopic kidney, ectopic testis and malformed kidney in fetuses at 100 mg/kg, when compared to concurrent and historical controls.) Previously reviewed as unacceptable (Becker, 12/1/87.) upon evaluation of the requested data, the study has been upgraded to acceptable with **possible adverse effects.** M. Silva, 11/13/95.

010 51078 Pilot study for 51080. (See 51080 worksheet for review.)

034 118537, supplemental to 51080.

GENE MUTATION

** 025 086791, "Salmonella Mutagenicity Tests: II. Results from the Testing of 270 Chemicals", (Mortelmans, K., Haworth, S., Lawlor, T., Speck, W., Tainer, B. and Zeiger, E., SRI International, Midwest Research Institute. Environmental Mutagenesis 8(7):1-119, 1986). o-Benzyl-p-chlorophenol (96.9% pure) was used on Salmonella typhimurium strains TA100, TA98, TA1535 and TA1537 at control (DMSO), 0.3, 1.0, 3.3, 10.0, 33.0 and 100.0 ug/plate at EG & G Mason Research Institute (EGG), or 0 (DMSO), 0.10, 0.30, 1.0, 3.0, 10.0, 33.0, 66.0, 100.0 ug/plate at Stanford Research Institute (SRI). Plates were run in triplicate. All strains were tested with and without S9 (from Aroclor 1254 induced male Sprague-Dawley rat and male Syrian hamster livers). Preincubation of the test chemical with the tester strain in either buffer or S9 for 20 minutes at 37:C prior was performed (two trials/study). No increase in the reversion rate was reported. ACCEPTABLE**.** (M. Silva, 6/18/91).

025 086791, "Salmonella Mutagenicity Tests: II. Results from the Testing of 270 Chemicals", (Mortelmans, K., Haworth, S., Lawlor, T., Speck, W., Tainer, B. and Zeiger, E., SRI International, Midwest Research Institute. Environmental Mutagenesis 8(7):1-119, 1986). o-Benzyl-p-chlorophenol (96.9% pure) was used on Salmonella typhimurium strains TA98, TA100, TA1535 and TA1537 (duplicate or triplicate cultures) in a mutagenesis assay (with and without S9 from Aroclor 1254 induced male Sprague-Dawley rat and male Syrian hamster livers). Dose levels were: 0 (DMSO), 0.1, 0.3, 1.0, 3.0, 3.3, 10.0, 33.0, 66.0, or 100.0 ug/plate. No increase in the reversion rate was reported. Supplemental information. (H. Green & M. Silva, 6/18/91).

CHROMOSOME ABERRATIONS

** 043 131516, "Chromosome Aberrations in Chinese Hamster Ovary (CHO) Cells", (D.L. Putman and P.T. Curry, Microbiological Associates, Inc., Blackwell Rockville, MD., Report # 93-C500-SW, 18 May 1994). The test article is identified as 2-benzyl-4-chlorophenol with 99.7% purity. Chinese Hamster ovary (CHO-K1) cells were exposed in duplicate without activation at untreated, 0 (DMSO), 4.0, 8.0, 15.0, 30.0, and 60.0 ug/ml (20 hours) and in the presence of activation at untreated, 0 (DMSO), 1.3, 2.5, 5.0, 10.0, and 20.0 ug/ml (2 hours). **An increase in chromosomal aberrations was not observed at any dose**. **Acceptable**. (Green & Silva, 11/6/95).

025 086792, "National Toxicology Program, In Vitro Cytogenetic Testing of Ortho Benzyl Parachlorophenol", (D. K. Gulati, Ph.D., Litton Bionetics, Inc., Environmental Health and Research Testing, September, 1989). o-Benzyl-p-chlorophenol (characteristics not provided) was tested for sister chromatid exchange and chromosomal aberrations in Chinese hamster ovary (CHO) cells both with and without S-9 (Aroclor induced male Sprague-Dawley rat livers) at 0 (DMSO), 0.050, 0.160, 0.500, 1.600, 5.000, 16.0, 17.9, 49.7, 149, 497, 499, 596, 700, 745, 801, or 14900 ug/ml. No increase in chromosomal aberrations or sister chromatid exchanges was reported. This report is considered supplementary information which can possibly be upgraded upon submission of the entire report (chemical characteristics, full protocol describing evaluation of SCE and chromosomal aberrations, individual data/group). (H. Green & M. Silva, 6/24/91)

001 013552, summary information.

DNA DAMAGE

** 026 091229, "Assessment of Clastogenic Action on Bone Marrow Erythrocytes in the Micronucleus Test", (C. N. Edwards, Life Science Research Limited, Eye, Suffolk IP23 7PX, England, Report # 90/NLL035/0169, 2/7/90). Nipacide BCP (0-benzyl-p-chlorophenol, 97.9% pure) was used in an in vivo micronucleus test and administered by gavage at 0 (maize oil), 250, 500, 1000, or 2000 mg/kg to 5 or 15 CD-1 mice/sex/group. 2000 erythrocytes/animal were examined and the frequency of micronucleated cells/1000 polychromatic erythrocytes was scored. A treatment-related increase in micronuclei was not reported. ACCEPTABLE. (H. Green & M. Silva, 6/14/91).

SUPPLEMENTAL INFORMATION

Subchronic Studies:

024 086790, "Prechronic Toxicity of o-Benzyl-p-Chlorophenol in Rats and Mice", (Birnbaum, L.S., Deskin, R., Grumbein, S.L., Kurtz, P., Fowler, K.L. and Peters, A.C., National Toxicology Program, Battelle Columbus Division, Columbus, OH., published in Fundamental and Applied Toxicology 7, 615-625 (1986)). o-Benzyl-p-chlorophenol (97.5% pure) was used on F344 rats and B6C3F1 mice in acute, subacute (12 exposures administered over a 16 day period) to 3 (rats) or 4 (mice) day period), and subchronic (13 week) gavage studies. Acute doses (5 rats or mice/sex/dose) were 250, 500, 1000, 2000, and 4000 mg/kg. Subacute doses (5 rats or mice/sex/dose) were 0 (corn oil), 62.5, 125, 250, 500, or 1000 mg/kg. Subchronic levels (mice) were 0 (corn oil), 500, 650, 800, or 1000 mg/kg/day and (rats) 0 (corn oil), 30, 60, 120, 240, and 480 mg/kg/day (10/sex/dose).
Results Acute: 90-100% mortality at ≥ 2000 mg/kg (rats & mice). Zero and 10% mortality in mice & rats at 1000 mg/kg respectively. Clinical signs were diarrhea, piloerection, hypo- and hyperactivity. No gross lesions were visible at autopsy.
Results Subacute: reduced food consumption (27% both sexes) and body weight gain (-116% in males and -70% in females) for rats at 1000 mg/kg. Females at 500 mg/kg showed a 23% decrease in

body weight gain and a 15% decrease in food consumption. No effects on food consumption or body weight were reported in mice. Clinical signs were diarrhea and rough haircoat in rats and rough haircoat and crouched or hunched posture in mice. Necropsy revealed dose related increase in absolute kidney, liver and brain weights and a decrease in absolute thymus and heart weights in rats at ≥ 500 mg/kg. Histopathology showed kidney nephrosis (all rats at 1000 mg/kg), including multifocal individual epithelial necrosis, tubular regeneration and hyaline cast formation in the renal cortex (dose related). Similar lesions were noted in mice at ≥ 500 mg/kg. In both strains, cecal dilatation was accompanied by necrosis.

Results Subchronic: Mortality reported was due to gavage errors. Rats showed an absolute thymus weight decrease and an increased kidney weight at 480 mg/kg (males) and ≥ 240 mg/kg (females). There were no dose-related lesions at necropsy, however, histopathology showed multifocal dilatation of renal tubules, flattening of the epithelium, hyaline casts and occasional foci of mononuclear cells in the cortical interstitium (males at ≥ 240 mg/kg and in females at 480 mg/kg. Thymic lymphoid depletion was also observed in 8/10 females and 1/10 males at 480 mg/kg. Mice showed 19/20 at 1000 mg/kg and 14/20 at 800 mg/kg died prior to study termination. Clinical signs showed hypoactivity or lethargy and a rough or oily haircoat at ≥ 650 mg/kg. Male mice showed increased liver weight at 800 mg/kg and females at ≥ 500 mg/kg. Males showed a decrease in kidney weight at ≥ 650 mg/kg (no effect in females). Histopathology showed renal tubule necrosis, casts, chronic inflammation of the interstitium and renal tubule regeneration at all treatment levels (both sexes).

Discussion: Effects in the thymus from the repeated dose, subacute were considered in the report to be due to stress, rather than OBPC exposure per se. It was also stated that the cecal dilation was compatible with the germicidal nature of OBPC.

According to the report, the nephrotoxicity observed in rodents, due to OBPC treatment, may be related to the persistence of metabolites in the kidney. In addition, this compound has been reported to alter drug-metabolizing abilities of kidney in rats. Rats were more sensitive than mice to the nephrotoxic effects of OBPC. In contrast to other structurally related phenolic disinfectants OBPC does not appear to be neurotoxic or immunosuppressive.

AN ADDITIONAL SUPPLEMENT SHOWED DATA FROM A CHRONIC STUDY (no protocol or explanation was included). The study was conducted by Battelle Laboratories, Columbus, OH (8/87) for the National Toxicology Program.

Fischer 344 rats (50/sex/dose, plus 20/sex/dose for satellite groups) were gavaged with OBPC at 0, 60, 120, and 240 mg/kg and B6C3F1 mice (50/sex/dose plus 20/sex/dose for satellite groups) were gavaged at 0, 120, 240 and 480 mg/kg for 102 (rats) or 104 (mice) weeks. Test result tables for histopathology and mortality were included. Mortality rates were acceptable for both strains. **FOR RATS**, there was a statistically significant increase in adrenal medullary benign pheochromocytomas, epithelial adenoma in kidney, renal tubule tumors (either adenoma, carcinoma or adenocarcinoma), mammary gland tumors (either fibroma, fibroadenoma, carcinoma, adenocarcinoma or adenoma), uterine stromal polyp, and uterine stromal sarcoma or stromal polyp. The tumors occurred in both sexes, except the mammary gland and uterine tumors. Oncogenic NOEL rats ≤ 60 mg/kg (oncogenic effects were noted at all doses, primarily in females). **MICE:** There were no significant increases in oncogenic effects in mice.

(H. Green & M. Silva, 6/25/91).

024 086829, "Supplement No. 2, Prechronic Toxicity Study in Rats and Mice (O-Benzyl-p-chlorophenol)", (Randy Deskin, Ph.D., National Toxicology Program, Battelle Columbus Division, Columbus, OH., 1983). o-Benzyl-p-chlorophenol (characteristics not provided) was administered by gavage to F344 rats in three studies: **Acute:** 0 (corn oil), 250, 500, 1000, 2000, and 4000 mg/kg (5/sex/group). **Repeated Dose:** A total of 12 doses over 3 consecutive days at 0 (corn oil), 62.5, 125, 250, 500, and 1000 mg/kg. **Subchronic:** 0 (corn oil), 30, 60, 120, 240 or 480 mg/kg (10/sex/dose) for 13 weeks. **Acute Results:** Mortality showed # deaths/# dosed = 0/10, 0/10, 1/10 (1

female), 9/10 (5 females), and 9/10 (5 females) at 250, 500, 1000, 2000, and 4000 mg/kg respectively. Clinical signs included hypoactivity and diarrhea (≥ 2000 mg/kg), piloerection (≥ 500 mg/kg), and hyperactivity (≥ 1000 mg/kg). Necropsy revealed a discolored thymus (both sexes). **Repeated Dose NOEL** = 125 mg/kg (Clinical signs, at 1000 mg/kg showed diarrhea, wet tail area, and rough haircoat in both sexes. A decrease in body weight gain was reported in both sexes at 1000 mg/kg. Food consumption was depressed in both sexes at 1000 mg/kg. Mean liver/body weight ratios for males at ≥ 500 mg/kg and in females at 1000 mg/kg were increased. Thymus/body weight ratios in males at ≥ 500 mg/kg and in females at ≥ 250 mg/kg and thymus/brain weights at ≥ 500 mg/kg (both sexes) were decreased. Liver and kidney/brain weight ratios (females) at 1000 mg/kg were increased. Nephrosis and dilatation in the cecum at ≥ 250 mg/kg and necrosis of the epithelium of the cecum at ≥ at 250 mg/kg, and hemorrhage of the cecum was in 1 rat at 500 mg/kg. Epithelial necrosis, tubular regeneration and hyaline cast formation were also reported in kidney at 1000 mg/kg.) **Subchronic NOEL** = 125 mg/kg (A brownish discoloration of the haircoat around the penis, a reddish-yellow staining around the uro-genital area (females), tunnelling behavior, excessive hair loss and diarrhea were reported at ≥ 240 mg/kg. Organ/body and organ/brain weight ratios showed kidney increased and thymus decreased. Necropsy reported dose-related multifocal dilatation of the renal tubules, with flattening of the epithelium, hyaline casts and occasional foci of mononuclear cells in the cortical interstitium.) **Supplemental**. (H. Green & M. Silva, 6/25/91)

Dermal Study:

**** 025 086793**, "(Ortho-Benzyl Parachlorophenol), 21-Day Percutaneous Toxicity Study in the Rabbit", (H. A. Cummins, Life Science Research Limited, Eye, Suffolk IP23 7PX, England, 9/20/89). o-Benzyl-p-chlorophenol (Chlorophen; chemical characteristics not included) was used on clipped skin of New Zealand white rabbits (7/sex/group) in a daily occluded exposure for 21 consecutive days (6 hours/day) at 0 (50% v/v aqueous ethanol), 1, 5, and 25 mg/kg/day. **Possible adverse effects** indicated. Dermal NOEL = 1 mg/kg/day (Moderate or mild dermal irritation was reported at 5 mg/kg/day with dermal necrosis evident at 25 mg/kg/day). Systemic NOEL ≥ 25 mg/kg/day. Acceptable, however, a characterization of the technical material is requested. (H. Green & M. Silva, 6/24/91)

042 131245 "Dermal Absorption of 14-C-O-Chlorophenol From a 5% Formulation," (D.L. Warren, Miles Inc., Stilwell, KS; Study #: 94-722-XC; 6/28/94). BCP, used as NIPA BCP Disinfectant (5% a.i.) was administered to adult male Sprague-Dawley rats (16/dose) at 0.3, 3 and 30 mg/kg (a.i.) for 1, 4, 10 or 168 hours (4 sacrificed/dose/time-point). At 1 & 4 hours, skin was wiped prior to sacrifice. However, the group designated for the 168 hour sacrifice was wiped at 10 hours but not immediately prior to sacrifice. Controls (water only) were added as needed (for radioactivity). All animals were treated with 10 uCi (14C-BCP) and urine and feces were collected at pre-test, at termination for exposure times from 1 -10 hours and once/day for the 168 hour group. Data recovered from filters showed little volatilization of compound. Absorption is not complete (approximately 34-38% at 10 hours and 51% at 168 hours) through skin. Data suggest that BCP bound to skin eventually moves into the body. Radioactivity collected in urine, feces and cage wash showed that most BCP was eliminated in the first 10 hours (83%, 80% & 89%--urine and 10%, 10% and 31%--feces at 5, 50 and 500 ug/cm2, respectively). Cage wash was less than 3%. By 168 hours, most of the labeled material was in the feces and most of the material was passed by 2 days. These data are supplemental. M. Silva, 11/15/95.

040 127784 Initiation/Promotion Study of o-Benzyl-p-Chlorophenol in Swiss (CD-1) Mice (Mouse Skin Study), (NTP TR-444, NIH Publication #: 93-3157; Battelle, Columbus, OH, 11/16/93). BCP (97%) was administered to the dorsal interscapular region on the backs of Swiss CD-1 mice (50/sex/treatment) to test it as an initiator, promotor or complete carcinogen in the following series of experiments:

Dose Regimen in the 1-Year Initiation/Promotion Study of BCP[1]

Treatment		
Initiator[2]	**Promotor[3]**	**Test Group**
Acetone	Acetone	Vehicle Control
50 ug DMBA	Acetone	Initiator Control
5 ug TPA	5 ug TPA	Promotor Control
50 ug DMBA	5 ug TPA	Initiator/Promotor Control
Acetone	20 ug DMBA	Complete Carcinogen Control
10 mg BCP	5 ug TPA	Initiator
50 ug DMBA	0.1 mg BCP	Low-Dose Promotor
50 ug DMBA	1.0 mg BCP	Mid-Dose Promotor
50 ug DMBA	3.0 mg BCP	High-Dose Promotor
10 mg BCP	0.1 mg BCP	Low-Dose Complete Carcinogen
10 mg BCP	1.0 mg BCP	Mid-Dose Complete Carcinogen
10 mg BCP	3.0 mg BCP	High-Dose Complete Carcinogen

1 - All dose volumes were 100 ul.
2 - Initiator doses were applied once during week 1 of the study, at which time mice were approximately 56 days old.
3 - Except for TPA, promotor doses were applied three times per week from week 2 - 52. TPA was applied three times per week as a promotor for the first 6 months of the study and once per week for the last 6 months.
TPA = 12-o-tetradecanoylphorbol-13-acetate; DMBA = 7, 12-dimethylbenz(a)anthracene; BCP = o-benzyl-p-chlorophenol.

In addition, genotoxicity of BCP was tested in Salmonella typhimurium and cultured Chinese hamster ovary cells.

RESULTS OF BCP TESTED AS A COMPLETE CARCINOGEN: BCP functioned as an irritant when used as a single initiating dose of 10 mg, followed by repetitive applications of 0.1, 1.0 or 3.0 mg BCP for 52 weeks. Many mice developed cutaneous lesions of scaling/crusts and ulceration. There was no increase in incidence in neoplasms at the application sites of any BCP/BCP mice.

RESULTS OF BCP TESTED AS AN INITIATOR: One vehicle control (acetone/acetone) male mouse developed crusts at the site of application at necropsy, but no male or female vehicle controls developed papillomas. Mice administered BCP/TPA developed application site lesions, including scaling/crusts, ulceration and irritation. Incidences of these lesions were similar to those in initiator/promotor control (DMBA/TPA): 12/50 males had papillomas after 22 weeks; 7/50 females had papillomas after 11 weeks (BCP/TPA-treated mice). BCP/TPA mice had lower incidences of papillomas than mice administered TPA/TPA (16/50, males; 16/50, females) and much lower than those in DMBA/TPA mice (40/50, males; 48/50, females). The report stated that although incidences of papillomas in mice administered BCP as an initiator were significantly greater than those in the vehicle controls, they were not significantly different from those in TPA/TPA mice. Therefore, BCP was not considered an initiator.

RESULTS OF BCP TESTED AS A PROMOTOR: Dose-related increases in scaling and/or crusts, ulceration and irritation were observed at the site of application in DMBA/BCP-treated males and females. Incidences in scaling and/or crusts, ulceration and irritation in 3.0 mg BCP mice were similar to incidences in the DMBA/TPA (initiator/promotor) group but much higher than in the DMBA/acetone (initiator/control) group. According to the report, BCP was considered to have promotion potential because the incidences of papillomas in mice treated with DMBA/3.0 mg BCP were greater than those in the DMBA/acetone (initiator/control) mice and because topical exposure to BCP alone did not significantly increase the incidence of papillomas. Since incidences of papillomas in DMBA/3.0 mg BCP mice (14/50, males; 18/50, females) were much less than incidences in DMBA/TPA (promotor/control) mice (40/50, males; 48/50, females). The report considered BCP to be a weak promotor.

GENETIC TOXICOLOGY: BCP did not induce gene mutations in Salmonella typhimurium (TA98, TA100, TA1535 or TA1537) and did not induce sister chromatid exchanges or chromosomal aberrations in cultured CHO cells when tested with and without activation.

CONCLUSIONS: BCP was a cutaneous irritant and a weak promotor (relative to TPA) but was not an initiator or a complete carcinogen.
These data are supplemental. M. Silva, 11/14/95.